Agency for Healthcare Research and Quality
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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Management of abnormal cervical cancer screening test results and cervical cancer precursors.

Bibliographic Source(s)

American College of Obstetricians and Gynecologists (ACOG). Management of abnormal cervical cancer screening test results and cervical cancer precursors. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2013 Dec. 30 p. (ACOG practice bulletin; no. 140). [159 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American College of Obstetricians and Gynecologists (ACOG). Management of abnormal cervical cytology and histology. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Dec. 26 p. [169 references]

Recommendations

Major Recommendations

The grade of evidence (I–III) and level of recommendation (A–C) are defined at the end of the "Major Recommendations" field.

The following recommendations are based on good and consistent scientific evidence (Level A):

- For women with atypical squamous cells of undetermined significance (ASC-US) cytology test results, reflex human papillomavirus (HPV) testing is preferred.
- For women with HPV-positive ASC-US, whether from reflex HPV testing or co-testing, colposcopy is recommended.
- For women with low-grade squamous intraepithelial lesion (LSIL) cytology test results and no HPV test or a positive HPV test result, colposcopy is recommended.
- For women with a histologic diagnosis of cervical intraepithelial neoplasia (CIN) 2, CIN 3, or CIN 2,3 and adequate colposcopic examination, both excision and ablation are acceptable treatment modalities, except in pregnant women and young women.

The following recommendations are based on limited and inconsistent scientific evidence (Level B):

- For women 30 years of age and older with HPV-positive but cytology-negative co-test results, repeat co-testing at 1 year is acceptable. For women with HPV-negative ASC-US, whether from reflex HPV testing or co-testing, repeat co-testing at 3 years is recommended.
- When colposcopy does not identify CIN in women with HPV-positive ASC-US, co-testing at 12 months is recommended. If the co-test result is HPV-negative and cytology negative, return for age-appropriate testing in 3 years is recommended.

- For women aged 21 to 24 years with ASC-US cytology test results, cytology testing alone at 12-month intervals is preferred, but reflex HPV testing is acceptable.
- For women aged 65 years and older, HPV-negative ASC-US test results should be considered abnormal when considering discontinuation of screening.
- For women aged 21 to 24 years with LSIL cytology test results, follow-up with cytology testing at 12-month intervals is recommended. Colposcopy is not recommended.
- For pregnant women with LSIL, colposcopy is preferred.
- For women with atypical squamous cells, cannot exclude high-grade squamous intraepithelial lesions (ASC-H) cytology test results, colposcopy is recommended regardless of HPV result. Reflex HPV testing is not recommended.
- For women with high-grade squamous intraepithelial lesion (HSIL) cytology test results, immediate loop electrosurgical excision procedure (LEEP) or colposcopy is acceptable, except in special populations.
- A diagnostic excisional procedure is recommended for women with HSIL cytology test results when the colposcopic examination is inadequate, except during pregnancy.
- For women aged 21 to 24 years with ASC-H or HSIL test results, colposcopy is recommended. Immediate treatment (i.e., see-and-treat) is unacceptable.
- For women with all subcategories of atypical glandular cells (AGC) and adenocarcinoma in situ (AIS) except atypical endometrial cells, colposcopy with endocervical sampling is recommended regardless of HPV test result. Endometrial sampling is recommended in conjunction with colposcopy and endocervical sampling in women 35 years of age and older with all subcategories of AGC and AIS. Endometrial sampling is also recommended for women younger than 35 years with clinical indications that suggest they may be at risk of endometrial neoplasia.
- No further evaluation is recommended for asymptomatic premenopausal women with benign endometrial cells, endometrial stromal cells, or histiocytes. For postmenopausal women with benign endometrial cells, endometrial assessment is recommended regardless of symptoms.
- For women aged 25 years and older with CIN 1 or no lesion preceded by "lesser abnormalities," co-testing at 1 year is recommended. If both the HPV test and cytology test results are negative, then age-appropriate retesting 3 years later is recommended. If all test results are negative, then return to routine screening is recommended. If any test result is abnormal, then colposcopy is recommended. If CIN persists for at least 2 years, either continued follow-up or treatment is acceptable.
- When CIN 1 is detected on endocervical sampling after lesser abnormalities but no CIN 2+ is detected colposcopically directed biopsies, management should follow American Society for Colposcopy and Cervical Pathology (ASCCP) management guidelines for CIN 1, with the addition of repeat endocervical sampling in 12 months.
- For women aged 21 to 24 years with CIN 1 after an ASC-US or LSIL cytology test result, repeat cytology testing at 12-month intervals is recommended. Follow-up with HPV testing is unacceptable.
- Regardless of antecedent cytology test results, treatment of CIN 1 in women aged 21 to 24 years is not recommended.
- Treatment of pregnant women for CIN 1 is unacceptable.
- Hysterectomy is unacceptable as primary therapy for CIN 2, CIN 3, or CIN 2,3.
- For women treated for CIN 2, CIN 3, or CIN 2,3, co-testing at 12 months and 24 months is recommended. If both co-test results are negative, retesting in 3 years is recommended. If any test result is abnormal, colposcopy with endocervical sampling is recommended. If all test results are negative, routine screening is recommended for at least 20 years, even if this extends screening beyond 65 years of age.

The following recommendations are based primarily on consensus and expert opinion (Level C):

- For women with an unsatisfactory cytology test result and no, unknown, or a negative HPV test result, repeat cytology testing in 2 to 4 months is recommended.
- For women aged 21 to 29 years with negative cytology test results and absent or an insufficient endocervical–transformation zone component, routine screening is recommended. For women aged 30 years and older with cytology test results reported as negative and with an absent or insufficient endocervical–transformation zone component and no or unknown HPV test result, HPV testing is preferred.
- Acceptable options for the management of postmenopausal women with LSIL and no HPV test include obtaining HPV testing, repeat cytology testing at 6 months and 12 months, and colposcopy.
- For women aged 21 to 24 years with HSIL cytology test results, when CIN 2+ is not identified on histology testing, observation for up to 24 months using both colposcopy and cytology testing at 6-month intervals is recommended, provided the colposcopic examination is adequate and endocervical assessment is negative or CIN 1.
- When CIN 2+ is not identified on histologic testing, either a diagnostic excisional procedure or observation with co-testing at 12 months and 24 months is recommended, provided in the latter case that the colposcopic examination is adequate and the endocervical sampling is negative. In this circumstance, it is acceptable to review the cytologic, histologic, and colposcopic findings.
- For women aged 21 to 24 years with CIN 1 or no lesions after an ASC-H or HSIL cytology test result, observation for up to 24 months using both colposcopy and cytology testing at 6-month intervals is recommended, provided the colposcopic examination is adequate and

endocervical assessment is negative.
- If CIN 2, CIN 3, or CIN 2,3 is identified at the margins of a diagnostic excisional procedure or in an endocervical sample obtained immediately after the procedure, reassessment using cytology testing with endocervical sampling at 4 to 6 months after treatment is preferred.
- For young women with a histologic diagnosis of CIN 2,3 not otherwise specified, either treatment or observation for up to 12 months using both colposcopy and cytology testing at 6-month intervals is acceptable, provided the colposcopy finding is adequate. When a histologic diagnosis of CIN 2 is specified for a young woman, observation is preferred but treatment is acceptable. Hysterectomy is preferred for women who have completed child-bearing and have a histologic diagnosis of AIS on a specimen from a diagnostic excisional procedure.

Definitions:

Grades of Evidence

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Levels of Recommendations

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

Clinical Algorithm(s)

The following algorithms are provided in the original guideline document:

- Management of women ≥ age 30, who are cytology negative, but HPV positive
- Management of women with atypical squamous cells of undetermined significance (ASC-US) on cytology
- Management of women with low-grade squamous intraepithelial lesions (LSIL)
- Management of women ages 21-24 years with either atypical squamous cells of undetermined significance (ASC-US) or low-grade squamous intraepithelial lesion (LSIL)
- Management of women with high-grade squamous intraepithelial lesions (HSIL)
- Management of women ages 21-24 yrs with atypical squamous cells, cannot rule out high grade SIL (ASC-H) and high-grade squamous intraepithelial lesion (HSIL)
- Initial workup of women with atypical glandular cells (AGC)
- Management of women with no lesion or biopsy-confirmed cervical intraepithelial neoplasia—grade 1 (CIN1) preceded by "lesser abnormalities"
- Management of women with no lesion or biopsy-confirmed cervical intraepithelial neoplasia—grade 1 (CIN1) preceded by ASC-H or HSIL cytology
- Management of women ages 21-24 with no lesion or biopsy-confirmed cervical intraepithelial neoplasia—grade 1 (CIN1)
- Management of young women with biopsy-confirmed cervical intraepithelial neoplasia—grade 2,3 (CIN 2,3) in special circumstances
- Management of women with biopsy-confirmed cervical intraepithelial neoplasia—grade 2 and 3 (CIN 2,3)

Scope

Disease/Condition(s)

- Human papillomavirus (HPV) infection
- Cervical abnormalities and cervical cancer precursors including:
  - Atypical squamous cells of undetermined significance (ASC-US)
  - Low-grade or high-grade squamous intraepithelial lesions (LSIL or HSIL)
  - Atypical squamous cells, cannot rule out HSIL (ASC-H)
  - Atypical glandular cells (AGC)
  - Adenocarcinoma in situ (AIS)
  - Cervical intraepithelial neoplasia (CIN)

Guideline Category

Diagnosis

Management

Risk Assessment

Screening

Treatment

Clinical Specialty

Obstetrics and Gynecology

Oncology

Pathology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To aid practitioners in making decisions about appropriate obstetric and gynecologic care
- To present the most recent revisions to guidelines for managing abnormal cervical cancer screening test results and cervical cancer precursors
- To describe the Lower Anogenital Tract Squamous Terminology (LAST Project) and provide guidance on applying the new management guidelines with this terminology

Target Population

Women aged 21 and older with abnormalities during cervical cancer screening

Interventions and Practices Considered

1. Reflex human papillomavirus (HPV) testing

2. Colposcopy with directed biopsy
3. Cytology testing
4. HPV testing and cytology (co-testing)
5. Endocervical sampling
6. Excision and ablation
7. Repeat colposcopy or cytology
8. Observation with co-testing
9. Loop electrosurgical excision procedure (LEEP)
10. Endometrial sampling
11. Hysterectomy (for women with recurrent disease or who have completed child bearing)

Major Outcomes Considered

- 5-year cancer risk rate
- Recurrence rates
- Sensitivity and specificity of testing
- Predictive value of tissue sampling methods on progression to cervical cancer

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The MEDLINE database, the Cochrane Library, and the American College of Obstetricians and Gynecologists' own internal resources and documents were used to conduct a literature search to locate relevant articles published between January 2000 and April 2013. The search was restricted to articles published in the English language. Priority was given to articles reporting results of original research, although review articles and commentaries also were consulted. Abstracts of research presented at symposia and scientific conferences were not considered adequate for inclusion in this document. Guidelines published by organizations or institutions such as the National Institutes of Health and the American College of Obstetricians and Gynecologists were reviewed, and additional studies were located by reviewing bibliographies of identified articles. When reliable research was not available, expert opinions from obstetrician-gynecologists were used.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Studies were reviewed and evaluated for quality according to the method outlined by the U.S. Preventive Services Task Force (1989):

I: Evidence obtained from at least one properly designed randomized controlled trial.

II-1: Evidence obtained from well-designed controlled trials without randomization.

II-2: Evidence obtained from well-designed cohort or case-control analytic studies, preferably from more than one center or research group.

II-3: Evidence obtained from multiple time series with or without the intervention. Dramatic results in uncontrolled experiments also could be regarded as this type of evidence.

III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees.

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Analysis of available evidence was given priority in formulating recommendations. When reliable research was not available, expert opinions from obstetrician-gynecologists were used. See also the "Rating Scheme for the Strength of the Recommendations" field regarding Level C recommendations.

Rating Scheme for the Strength of the Recommendations

Based on the highest level of evidence found in the data, recommendations are provided and graded according to the following categories:

Level A—Recommendations are based on good and consistent scientific evidence.

Level B—Recommendations are based on limited or inconsistent scientific evidence.

Level C—Recommendations are based primarily on consensus and expert opinion.

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

Practice Bulletins are validated by two internal clinical review panels composed of practicing obstetrician-gynecologists generalists and sub-specialists. The final guidelines are also reviewed and approved by the American College of Obstetricians and Gynecologists (ACOG) Executive

Board.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

This Practice Bulletin is adapted with permission from the American Society for Colposcopy and Cervical Pathology (ASCCP) publication 2012 Updated Consensus Guidelines for the Management of Abnormal Cervical Cancer Screening Tests and Cancer Precursors.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of abnormal cervical cancer screening test results and cervical cancer precursors

Potential Harms

- Cytologic interpretation is subjective. Both the possibility of missed disease and the potential for overtreatment must be considered, and management must be individualized based on the patient's needs and future risks of high-grade disease and cancer.
- Some currently available human papillomavirus (HPV) tests lack a control for epithelial cellularity, so an HPV result may be falsely negative because of an insufficient sample.
- Excisional treatments for cervical intraepithelial neoplasia (CIN) are associated with an increased risk of preterm delivery.
- For women who wish to maintain fertility, close observation after a deep conization is an option, but it carries a risk of persistent adenocarcinoma in situ (AIS) of up to 10% and a small risk of cancer even when the cone excisional margins are negative.
- Endocervical curettage can cause laceration of the soft cervix with consequent hemorrhage or rupture the amniotic membranes.
- Biopsy during pregnancy has not been linked to fetal loss or preterm delivery, whereas failure to perform biopsies during pregnancy has been linked to missed invasive cancer.
- Different terminologies for biologically equivalent lesions created a potential for miscommunication among pathologists and clinicians and increased the risk of overtreating patients.
- Currently available management strategies cannot eliminate the risk of developing cancer, and attempts to completely eliminate risk often result in unanticipated harm from excessive evaluation and overtreatment.

Contraindications

Contraindications

- Unless cancer is identified or suspected, treatment of cervical intraepithelial neoplasia (CIN) is contraindicated during pregnancy; CIN has no effect on the woman or fetus, whereas cervical treatments designed to eradicate CIN can result in fetal loss, preterm delivery, and maternal hemorrhage.
- Endocervical curettage is contraindicated during pregnancy

Qualifying Statements

Qualifying Statements

- The information is designed to aid practitioners in making decisions about appropriate obstetric and gynecologic care. These guidelines should not be construed as dictating an exclusive course of treatment or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to the institution or type of practice.
- There are several important principles in interpreting these guidelines. The revised guidelines were based on the best data available at the time of the 2012 consensus conference. Management strategies were developed based on risk where diagnoses with similar risk should have the same management. Clinical judgment is necessary in the application of these guidelines to individual patients. Currently available strategies cannot eliminate the risk of developing cancer, and attempts to completely eliminate risk often result in unanticipated harm from excessive evaluation and overtreatment.
- The guidelines apply to women identified with abnormalities during screening, and as with the 2006 guidelines, immunosuppressed women with abnormal results should be managed the same as immunocompetent women. Women with symptoms of a potential cervical disease require appropriate evaluation, which typically requires more than screening tests alone. In some instances, recommendations vary by age, particularly for 21 to 24 year olds. At other times, recommendations are specified for "young women," a definition (see Table 1 in the original guideline document) intended to reflect an individual woman's desire to minimize the effect of treatment on future pregnancy, and does not specify any particular age. Women younger than 21 years should not undergo screening. If a woman younger than 21 years is inadvertently screened and has an abnormal test result, the result should not be ignored and should be managed based on the guidelines for 21 to 24-year-old women.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Patient Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

American College of Obstetricians and Gynecologists (ACOG). Management of abnormal cervical cancer screening test results and cervical cancer precursors. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2013 Dec. 30 p. (ACOG practice bulletin; no. 140). [159 references]

Adaptation

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Date Released

2005 Sep (revised 2013 Dec)

Guideline Developer(s)

American College of Obstetricians and Gynecologists - Medical Specialty Society

Source(s) of Funding

American College of Obstetricians and Gynecologists (ACOG)

Guideline Committee

American College of Obstetricians and Gynecologists (ACOG) Committee on Practice Bulletins—Gynecology

Composition of Group That Authored the Guideline

This Practice Bulletin was developed by the Committee on Practice Bulletins—Gynecology with the assistance of Mark Spitzer, MD, and David Chelmow, MD.

American College of Obstetricians and Gynecologists (ACOG) committees are created or abolished and their overall function defined by the Executive Board. Appointments are made for one year, with the understanding that such appointment may be continued for a total of three years. The majority of committee members are Fellows, but Junior Fellows also are eligible for appointment. Some committees may have representatives from other organizations when this is particularly appropriate to committee activities. The president elect appoints committee members annually.

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: American College of Obstetricians and Gynecologists (ACOG). Management of abnormal cervical cytology and histology. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2008 Dec. 26 p. [169 references]

Guideline Availability

Electronic copies: None available

Print copies: Available for purchase from the American College of Obstetricians and Gynecologists (ACOG) Distribution Center, PO Box 933104, Atlanta, GA 31193-3104; telephone, 800-762-2264, ext. 192; e-mail: sales@acog.org. The ACOG Bookstore is available online at the ACOG Web site.

Availability of Companion Documents

None available

Patient Resources

The following are available:

- New guidelines for cervical cancer screening. Patient education fact sheet. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2013 Sep. 2 p. Available in Portable Document Format (PDF) from the American College of Obstetricians and Gynecologists (ACOG) Web site.
- Frequently asked questions: colposcopy. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2013 Jun. 2 p. Available in PDF from the ACOG Web site. Copies are also available in Spanish.
- Frequently asked questions: loop electrosurgical excision procedure. Washington (DC): American College of Obstetricians and Gynecologists (ACOG); 2013 Feb. 2 p. Available in PDF from the ACOG Web site. Copies are also available in Spanish.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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